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ANNUAL GENERAL MEETING M.S.S.V.D., 1937

The Sixteenth Annual General Meeting of the Society was held at Horton Hospital, Epsom, by kind permission of the Horton Hospital (L.C.C.) Sub-committee, on Saturday afternoon, July 10th. The President, Dr. H. M. Hanschell, was in the chair.

The Hon. Secretary read an epitome of the Minutes of the last annual General Meeting, which was approved; and the full Minutes, which were laid on the table for inspection, were signed.

In his report the Hon. Treasurer, Sir Frederick Menzies, K.B.E., stated that the total excess of the Society's assets over liabilities for the past year amounted to £401 15*s*. 4*d*. This sum does not include the half-share of the profits accruing from the publication of the Journal for the half-year ending June 30th, 1937, inasmuch as the statement from the publishers for this period was not at hand.

The Chairman announced that Sir Frederick Menzies had been reluctantly forced to the decision that he must relinquish his post of hon. treasurer, owing to the great pressure of the work for which he was responsible. The Hon. Secretary was requested to convey to Sir Frederick Menzies the appreciation of the Society for the great skill with which he had controlled the financial affairs of the Society for the last twelve years; his guidance had resulted in the placing of the conjoint affairs of the Society and of the *British Journal of Venereal Diseases* upon a most substantial basis.

Dr. Hanschell was re-elected into the post of President of the Society for the coming year, and the members whose names had been put forward by the Council for election into the other official posts were elected.

Dr. W. D. Nicol was elected into the post of Hon. Treasurer. Those who know him are in a position to congratulate the Society on the advent of one who will thus add to his reputation for efficiency, insight and sapiency.

Dr. W. D. Nicol and Dr. E. L. Hutton gave short addresses on Neurosyphilis. * A demonstration of patients referred to in the addresses was then given, and a most interesting collection of histological specimens dealing with the pathology of G.P.I., as arranged by Dr. A. D. Galbraith, and another series illustrative of the various phases of malaria in connection with the treatment of malaria, were shown. The latter specimens had been prepared by Mr. P. G. Shute with very great skill.

The President and Council of the Medical Society for the Study of Venereal Diseases wish to express their cordial thanks to Dr. Nicol for the valuable instruction extended to the members; and, further, to Mrs. Nicol and himself for their hospitality in entertaining the members to tea.

Mr. R. H. Curtis, Chief Officer of the Mental Hospital Department of the L.C.C. Committee, was present at the meeting, and to him the Society wish to express their gratitude for his sympathetic interest.

Addresses were given before the Society on April 30th, 1937, by Dr. W. D. NICOL and by Dr. E. L. HUTTON on the Treatment and Prophylaxis of Neurosyphilis.

I

Dr. Nicol showed some malaria charts to illustrate various points in regard to malaria therapy. Undoubtedly many cases occur in which a single inoculation with malaria fails and at some hospitals the practice is adopted of using some other pyrexial agent, such as T.A.B. vaccines. Charts were shown illustrating the very poor results obtained in some of these cases in which the amount of pyrexia was quite inadequate for therapeutic purposes. In these cases considerable delay occurs and, even if the patient does show mental improvement, a relapse comes on fairly soon after the treatment. Dr. Nicol also laid stress on the importance of adopting proper technique in using blood for inoculation. Sometimes there is too much delay before inoculation of the patient with blood, in which case the parasites are dead, and in others syringes and needles sterilised in spirit or other antiseptic are responsible for failure of the malarial

* Based upon their papers read before the M.S.S.V.D. on April 30th, 1937.

blood to react, by killing the parasites. The syringe employed for inoculation should either be dry sterilised or immersed in sterile normal saline. The second point raised was the question of immunity to the same strain, but there does not appear to be any immunity between different species of malaria ; consequently the knowledge of previous residence of any patient in a tropical country is of much value in deciding what species of malaria should be employed, and the use of a strain of Quartan in many cases who are immune to Benign Tertian malaria has proved extremely valuable in inducing a satisfactory course of therapy. At Horton, where some 800 cases had been treated, there had never been a failure of inoculating a European subject. There was only one instance of failure to inoculate a patient and that man was a West Indian negro in whom inoculations of Benign Tertian, Malignant Tertian, Quartan, Plasmodium Ovale and Plasmodium Knowlesi failed to give any true pyrexia. Charts of this man were shown and in spite of repeated inoculations, Quartan and P. Ovale parasites with very low pyrexia lasting only two or three days were found.

Finally, charts illustrating successful inoculations with different species of malaria in the same patient were shown.

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Dr. E. L. Hutton, speaking of the chronic cases of G.P.I., divided them into six groups as follows :—

(1) Patients with negative cerebro-spinal fluids, but whose mental condition necessitates permanent detention in a mental hospital. About 90 per cent. of the chronic G.P.I. population in Horton belongs to this group. In these cases malaria has been effective in arresting and possibly eliminating the syphilitic infection of the nervous system, but the subsequent clinical picture depends upon the degree of damage done to the brain cells by the spirochæte before the treatment was administered. The five cases shown in this group, all of whom were treated before August, 1926, illustrate the different mental and physical states which are produced and which can be correlated with the varying degree of irreparable parenchymatous degeneration ; one is arrested at a high mental level, with little mental deterioration and paranoid

symptoms, two show evidence of moderate dementia, one is grossly demented and one shows a slow progressive deterioration in spite of the negative fluid. In this latter case one would like to suggest that nervous tissue concerned with vital functions has been damaged, and that thus a vicious circle has been set up which persists though the actual infection has been " cured."

(2) This group illustrates the varying time periods which elapse before fluids become negative. In three of these patients the fluid when tested about two to two and a half years after treatment was still quite strongly positive, but in the ensuing eight months they became practically negative.

(3) Comprises patients whose fluids remain strongly positive after treatment. Of five patients shown, four are grossly demented, and two of these are definitely deteriorating. In one case the mental and physical condition is fairly good, but it is thought that this clinical remission will prove merely temporary, for it has been our experience that the ultimate fate of those in whom malaria does not restore the C.S.F. findings to normal is similar to that of the untreated G.P.I., and this is further confirmed by the similarity of the histopathological changes, spirochætes, positive iron reactions and perivascular infiltration being found in these, but not in patients with negative fluids.

(4) G.P.I. relapses following clinical remissions. There are four patients, of whom two had undoubtedly had inadequate treatment. The duration of the remission varied from one and a half to three years. All had positive C.S.F.s on readmission. A second course of malaria therapy has been given, but the prognosis is not good, though it might have been very satisfactory had the treatment been given before the reappearance of the mental symptoms. This emphasises the need for repeated C.S.F. investigations following treatment and the adoption of measures adequate to produce a completely negative fluid.

(5) Congenital G.P.I.s. Out of twenty-one congenital G.P.I.s admitted here only three have been discharged, and none of these made a complete recovery. Seven have died, while the remaining eleven are still in hospital. Two were treated as long as eleven years ago and five show practically negative C.S.F.s, one in whom the C.S.F.

remains strongly positive is deteriorating, while the rest have been treated too recently for the malaria to have produced any marked change in the fluid findings. Thus it seems probable that malaria is as effective in producing a negative C.S.F. in congenital syphilis as in acquired, but the poor clinical results are due to the irreparable nature of the damage done to the adolescent brain.

(6) Patients who had previously received anti-syphilitic treatment. These are included in order to remind those in charge of V.D. clinics that some of our failures are primarily their failures and that the timely use of the lumbar puncture needle might do much to reduce the numbers of the rapidly growing mental hospital population of treated but incurable general paralytics.

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The Histopathology of General Paralysis of the Insane

Notes describing a series of histo-pathological specimens demonstrated by A. J. Galbraith, M.D., D.P.M., (Horton Hospital, Epsom)

It must be realised from the onset that, apart from the demonstration of the *Spirochæta pallida* (which may be found in about 50 per cent. of untreated cases) in the brain tissue, there are no absolutely specific histological changes in general paralysis. The pathological processes which ensue represent the reactions of the central nervous system to an invading organism and its toxins, and similar changes if studied singly are just as typical for infections other than by *Sp. pallida*. Nevertheless, among the great variety of histopathological findings in dementia paralytica, it is possible to demonstrate combinations and localisations of lesions which are indicative of the disease process.

In macroscopical examination of the brain atrophy may be observed, and is usually restricted to the anterior parts, mostly to the frontal lobes. The meninges may be thickened, but only in chronic cases, and microscopically may show moderate degrees of cellular infiltration. The nerve cells of the cortex usually show various degenerative changes, and more severe changes consist of a general disturbance of the cytoarchitectonic structure

with small areas devoid of nerve cells (" dropping out ") and even gross destruction of the cortex, which gives rise to an appearance known as " spongy state." Again, these changes are largely confined to the anterior parts of the cerebral cortex. Another characteristic finding is that of perivascular infiltration of the intracerebral vessels with lymphocytes and plasma cells, giving a " cuffed " appearance to vessels. In connection with the blood vessels there arises a histochemical reaction of considerable importance, namely, the deposition of iron compounds in the adventitial cells and spaces. This reaction has been found to be positive in all untreated cases of G.P.I., is relatively rare in treated (malarial) cases, and has only been described elsewhere in trypanosomiasis and in a form of avian encephalitis. A brief discourse on the methods of demonstrating this iron reaction is by no means superfluous, as it represents an easy and reliable method of coming to a postmortem diagnosis of G.P.I. The Spatz test * is performed on fresh material, and a result can be obtained within a few minutes with the simplest appliances. More permanent preparations can be made by using the Turnbull method on alcohol-fixed, paraffin-embedded material. The iron reaction can be most usefully applied in cases where examination of the whole brain is not available, by making a puncture of the orbital plate through the upper part of the conjunctival sac and withdrawing a small amount of brain tissue by an instrument such as a surgical cannula or cork-borer.

The glial apparatus of the brain reacts in various ways, and typical findings are a subpial " felting " of glial fibres and proliferation of the macroglia and microglia with the formation of hypertrophied astrocytes and of Hortega " rod " cells.

The cornu ammonis is a region of the cerebrum which is particularly susceptible to toxic and other pathological processes, and, although well-marked histological changes occur in this region in G.P.I., it must be remembered that they commonly exist in many other pathological states. Such changes consist of gliosis, especially in the

* *Spatz Iron Reaction.*—Small pieces of brain tissue are received into normal saline and then placed in conc. ammonium sulphide for ten minutes, then washed well in water or saline, and a thin portion flattened between a slide and coverslip. The dark-green pigment can even be seen with a hand lens, and on higher magnification is observed to be localised in the adventitia of the blood vessels.

white matter of that region, increased lipoid content in the nerve cells, and also necrobiotic changes.

Myelin degeneration frequently occurs in all areas of the central nervous system in G.P.I. In the cortex there are two main types, viz., a diffuse demyelinisation affecting chiefly the supraradiary and tangential fibres, which give a characteristic " moth-eaten " appearance to stained specimens, and, secondly, a focal degeneration similar to that found in disseminated sclerosis. The changes in the cord may simulate the appearance of tabes dorsalis, of subacute combined degeneration or of disseminated sclerosis.

There are two further pathological changes which are associated with G.P.I. :—(i) Ependymal granulations, commonly known as " frosting," especially noticeable on the floor of the fourth ventricle, are almost invariably found in cases of G.P.I., but are in no way specific as is commonly asserted, and (ii) endarteritis, which may affect both cerebral and spinal vessels.

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NOTES BY MR. P. G. SHUTE (the Ministry of Health Laboratory at Horton Hospital)

At the demonstration, slides showing parasites of *P. vivax*, *P. falciparum*, *P. ovale*, and *P. malariæ* in both man and mosquito were exhibited.

Special attention was directed to two films of *P. vivax*, one, from a primary case, which showed two or more stages of development, and the other, from a relapse case, when only a single stage was present. In the former the fever is always quotidian while in the latter the fever is always tertian.

The demonstration called attention to the importance of evenly spread blood films, care being taken to ensure that the red corpuscles are nearly touching each other but not overlapping. By using a $\frac{1}{2}$ in. lens and a x6 eyepiece each microscope field consists of about four hundred red cells. Almost from the beginning of the practice of malaria therapy we have recognised that from the parasitological stand-point, one parasite per microscope field constitutes a reasonably heavy infection. This means that there are approximately 10,000 parasites

per cmm. We are definitely of the opinion that when two or more parasites per microscope field are present, particularly in the primary case, the attack should be aborted. An evenly spread film is of the utmost importance, otherwise, if, one day, a film is made where the red cells are overlapping and the next day the film is so thin that there are large spaces between the cells, parasite counts are meaningless. The demonstration showed a series of films prepared in this way.

The Horton standard model of routine staining was also demonstrated. It was pointed out that in order to obtain uniform results by Leishman's modification of Romanowsky's stain it is necessary

(1) to use a good reliable brand of methyl alcohol (acetone free) ;

(2) to use distilled water which is slightly alkaline ; we use water which is 7·2.

A series of slides showing malaria infected *Anopheles* at the Horton centre were also demonstrated. These included ex-flagellation of the male gametocyte, ookinetes, oocysts from the early stage to maturity and sporozoites from the salivary glands.

From 1925 until 1933 we used to collect out *Anopheles* from their natural haunts in nature, but following a series of experiments we have succeeded in breeding in the laboratory sufficient numbers for our work. The technique employed and the insectory was a feature of the demonstration.